

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
28 September 2000 (28.09.2000)

PCT

(10) International Publication Number
WO 00/56746 A3

(51) International Patent Classification⁷: C07H 9/04,
15/203 // 19/06, 19/16, 21/00

(21) International Application Number: PCT/DK00/00141

(22) International Filing Date: 24 March 2000 (24.03.2000)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
PA 1999 00407 24 March 1999 (24.03.1999) DK
PA 2000 00099 21 January 2000 (21.01.2000) DK

(71) Applicant (for all designated States except US): EXIQON
A/S [DK/DK]; Bygstubben 9, DK-2950 Vedbæk (DK).

(72) Inventors; and

(75) Inventors/Applicants (for US only): KOCHKINE,
Alexei [DK/DK]; c/o Jørgensen, Borgergade 26, apart-
ment 36, DK-1300 Copenhagen K (DK). FENSHOLDT,
Jef [DK/DK]; Ærtemarken 79, DK-2860 Søborg (DK).
PFUNDHELLER, Henrik, M. [DK/DK]; Dalgas Have
2, 4. tv., DK-2000 Frederiksberg (DK).

(81) Designated States (*national*): AE, AL, AM, AT, AT (util-
ity model), AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN,
CR, CU, CZ, CZ (utility model), DE, DE (utility model),
DK, DK (utility model), DM, DZ, EE, EE (utility model),
ES, FI, FI (utility model), GB, GD, GE, GH, GM, HR, HU,
ID, IL, IN, IS, JP, KE, KG, KP, KR, KR (utility model),
KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK,
MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI,
SK, SK (utility model), SL, TJ, TM, TR, TT, TZ, UA, UG,
US, UZ, VN, YU, ZA, ZW.

(84) Designated States (*regional*): ARIPO patent (GH, GM,
KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent
(AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent
(AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU,
MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM,
GA, GN, GW, ML, MR, NE, SN, TD, TG).

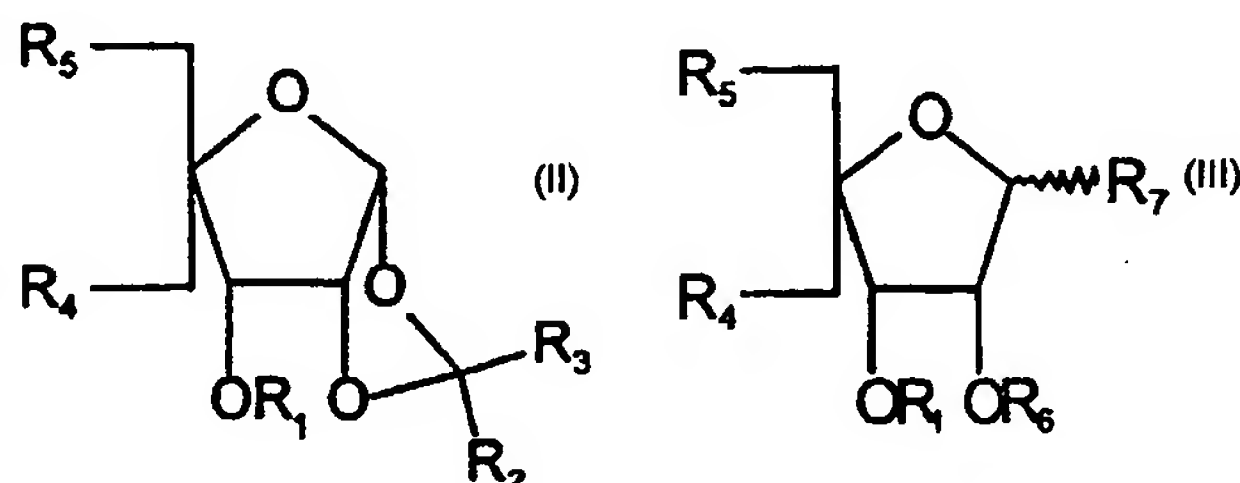
Published:

— with international search report

(88) Date of publication of the international search report:
18 October 2001

For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.

(54) Title: IMPROVED SYNTHESIS OF [2.2.1]BICYCLO NUCLEOSIDES



(57) Abstract: A synthesis of [2.2.1]bicyclo nucleosides which is shorter and provides higher overall yields proceeds via the key intermediate of general formula (III), wherein R₄ and R₅ are, for instance, sulfonates and R₇ is, for instance, a halogen or an acetate. From compounds in general formula (II), such as 3-*O*-aryl-4-*C*-hydroxymethyl-1,2-*O*-isopropylidene- α -D-ribofuranose, intermediates of general formula (III) are suitable for coupling with silylated nucleobases. Upon one-pot base-induced ring-closure and desul-

fonation of the formed [2.2.1]bicyclo nucleoside, a short route to each the LNA (Locked Nucleic Acid) derivatives of adenosine, cytosine, uridine, thymidine and guanidine is demonstrated. The use of the 5'-sulfonated ring-closed intermediate also allows for synthesis of 5'-amino- and thio-LNAs.

WO 00/56746 A3